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(12) **United States Patent**
Devellian et al.

(10) **Patent No.: US 9,216,014 B2**
(45) **Date of Patent: Dec. 22, 2015**

(54) **DEVICE WITH BIOLOGICAL TISSUE SCAFFOLD FOR PERCUTANEOUS CLOSURE OF AN INTRACARDIAC DEFECT AND METHODS THEREOF**

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(72) Inventors: **Carol A. Devellian**, Topsfield, MA (US); **Robert M. Carr**, Paradise Valley, AZ (US)

(73) Assignee: **W.L. Gore & Associates, Inc.**, Flagstaff, AZ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 291 days.

(21) Appl. No.: **13/893,270**

(22) Filed: **May 13, 2013**

(65) **Prior Publication Data**

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Related U.S. Application Data

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(51) **Int. Cl.**

A61B 1/32	(2006.01)
A61B 17/00	(2006.01)
A61B 17/12	(2006.01)

(52) **U.S. Cl.**

CPC ..... ***A61B 17/0057*** (2013.01); ***A61B 17/12122*** (2013.01); ***A61B 17/12172*** (2013.01); (Continued)

(58) **Field of Classification Search**

CPC A61B 17/0057; A61B 2017/00575; A61B 2017/00641; A61B 2017/00579; A61B 2017/00588; A61B 2017/00584; A61B 2017/00592; A61B 2017/00597; A61B 2017/00601; A61B 2017/00606

See application file for complete search history.

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Primary Examiner — Mary Hoffman

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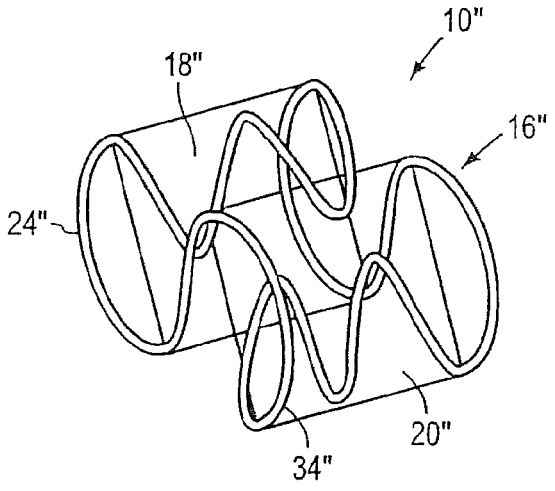
(57) **ABSTRACT**

The invention provides an intracardiac occluder, which has biological tissue scaffolds as occlusion shells, for the percutaneous transluminal treatment of an intracardiac defect. The intracardiac occluder includes a proximal support structure supporting the proximal occlusion shell and a distal support structure supporting the distal occlusion shell. In one embodiment, biological tissue derived from the tunica submucosa layer of the porcine small intestine forms the occlusion shells.

13 Claims, 8 Drawing Sheets



(52) **U.S. Cl.**
CPC *A61B2017/00575* (2013.01); *A61B 2017/00592* (2013.01); *A61B 2017/00606* (2013.01); *A61B 2017/1205* (2013.01); *A61F 2310/00365* (2013.01)

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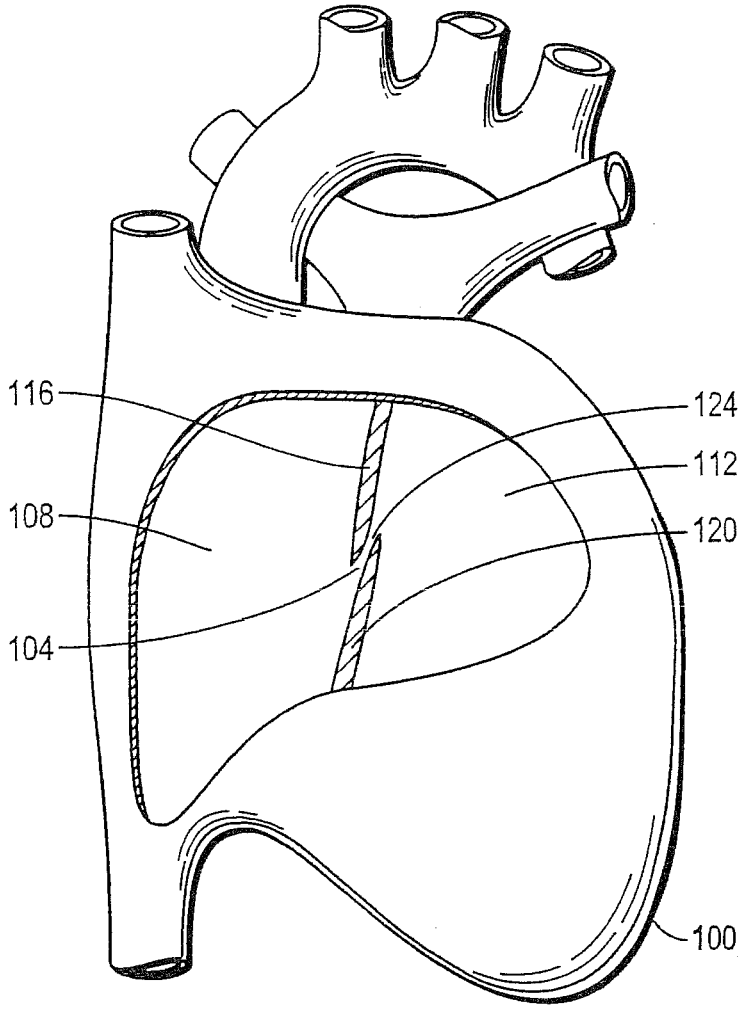

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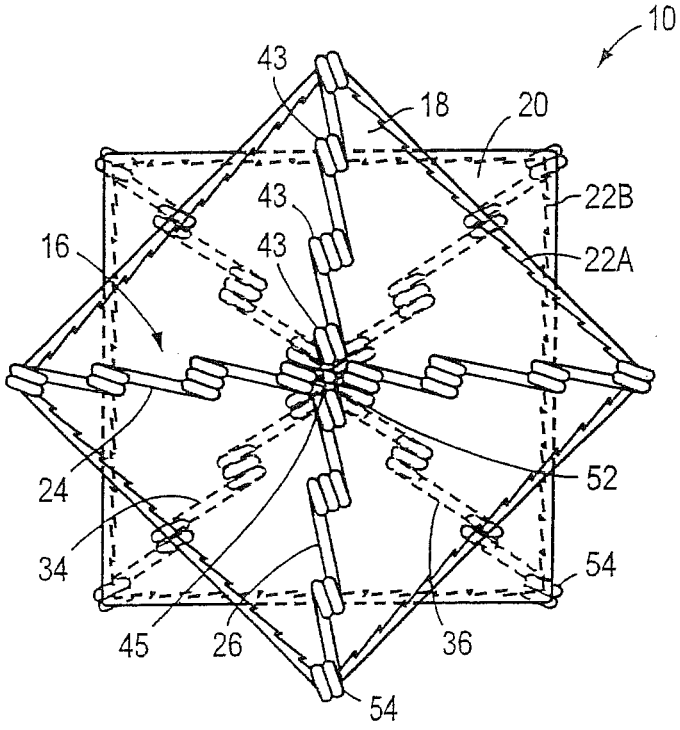
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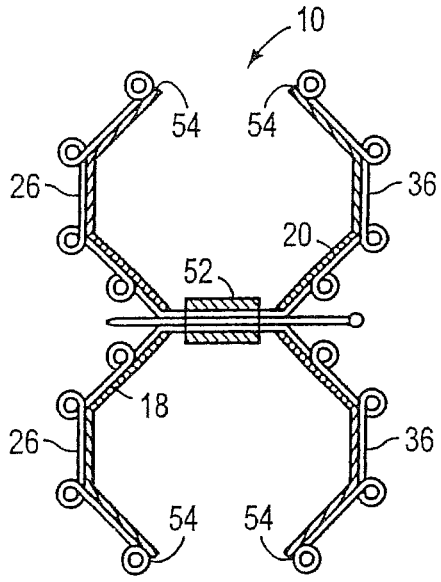
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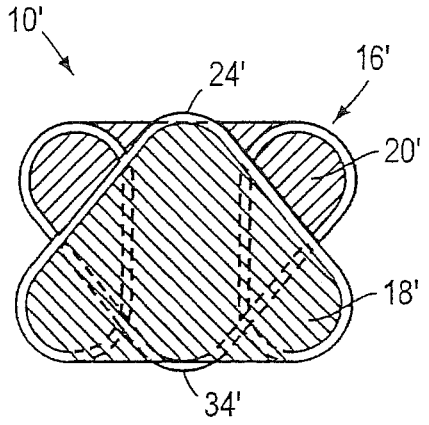
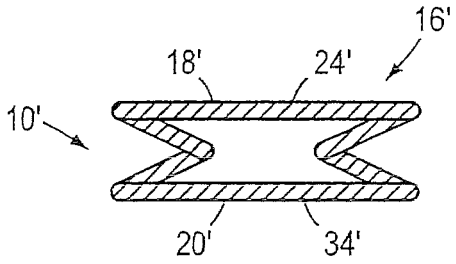


FIG. 3A



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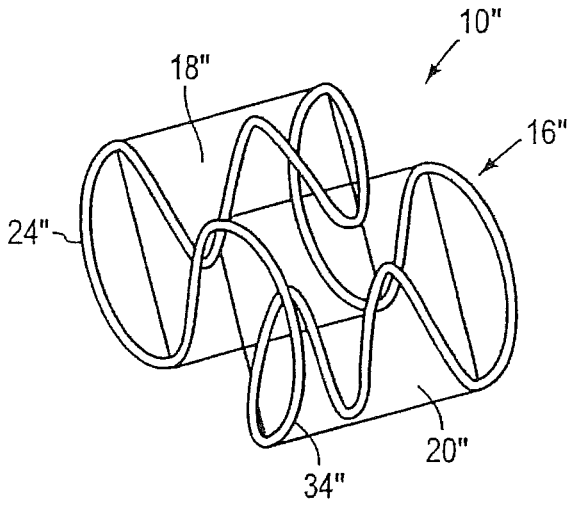

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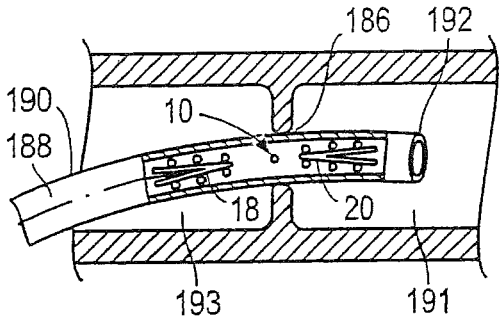


FIG. 5A

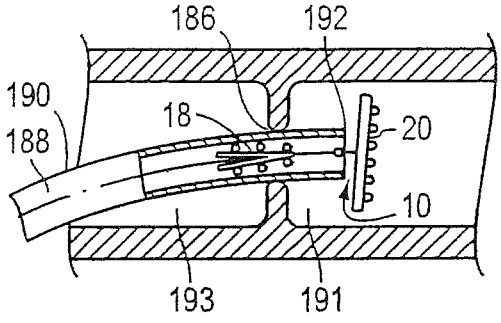


FIG. 5B

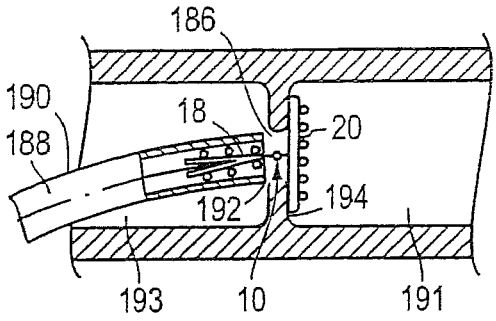


FIG. 5C

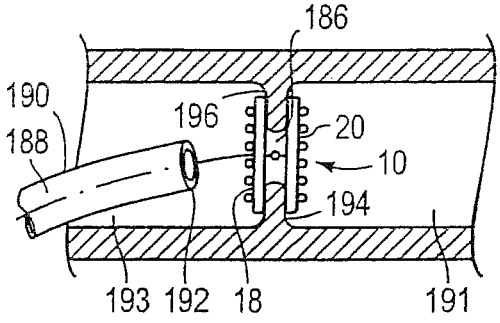


FIG. 5D

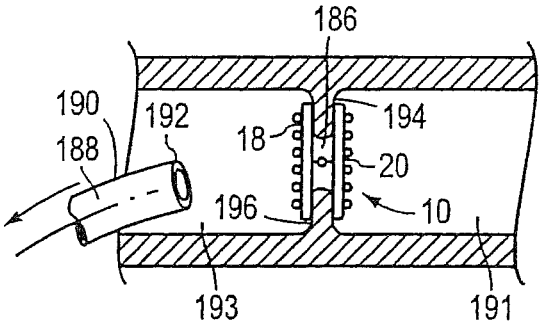
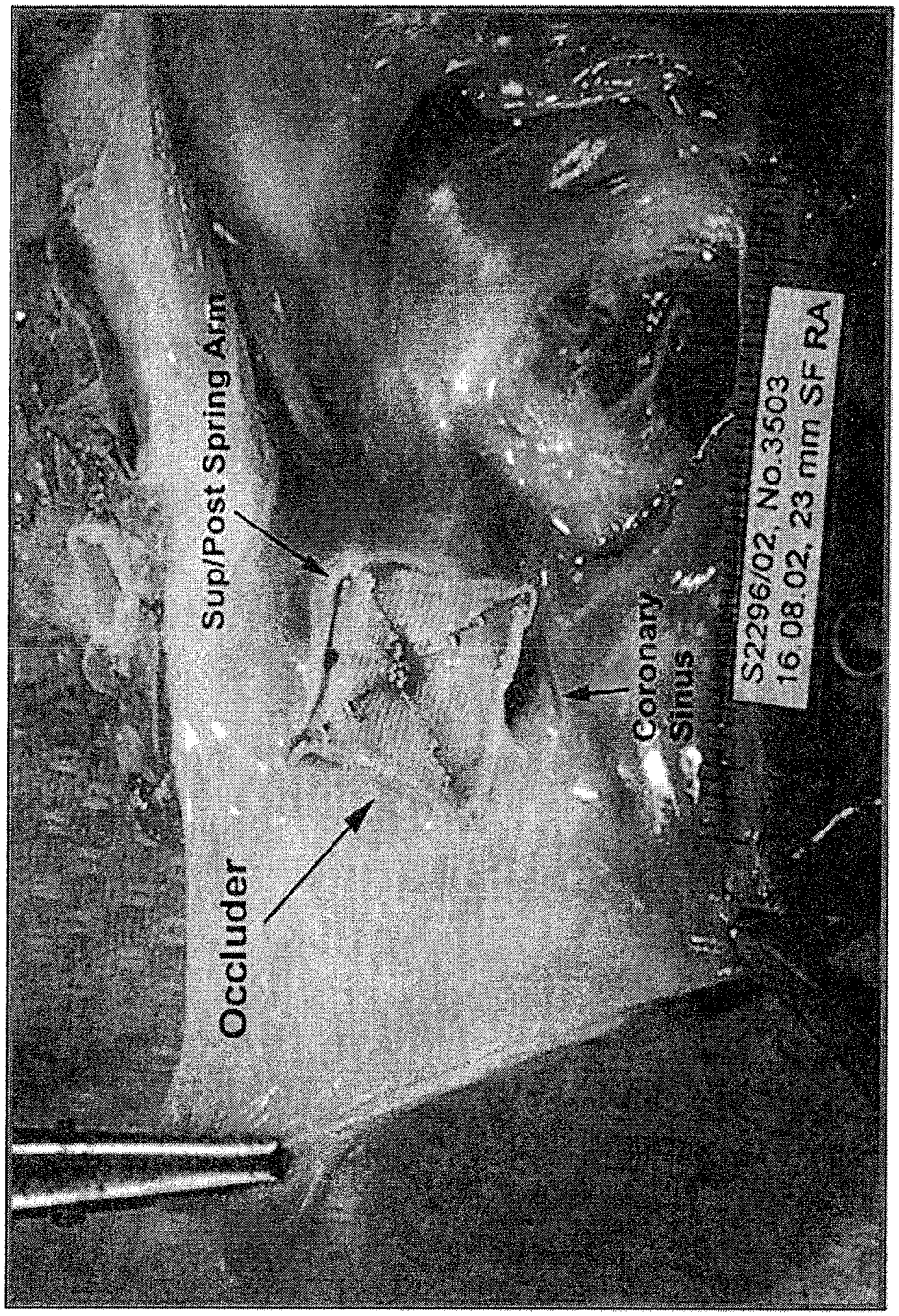


FIG. 5E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Sup/Post Spring Arm
Coronary Sinus
S2296/02, No.3503
16.08.02, 23 mm SF RA

FIG. 6A

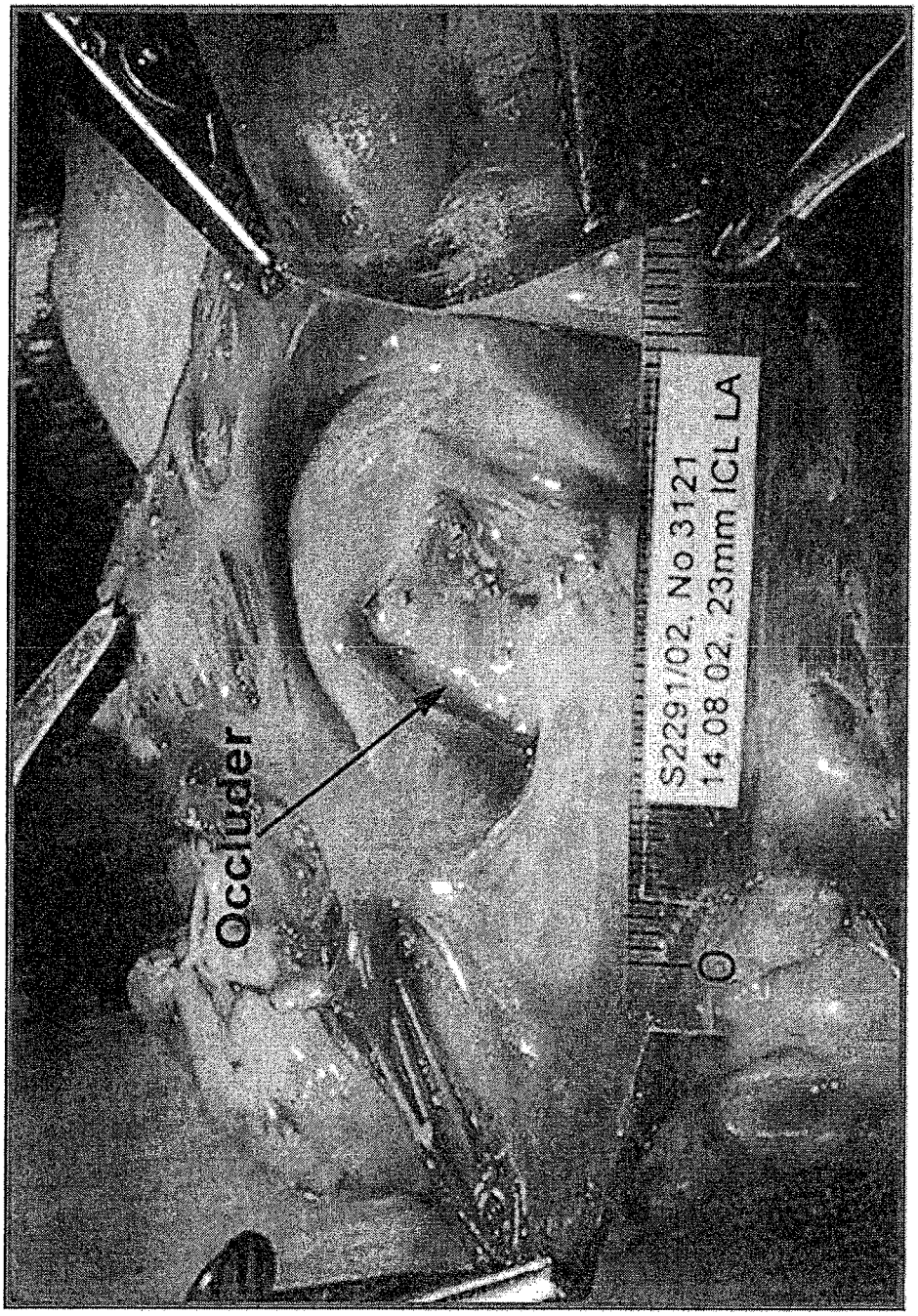

FIG. 6B

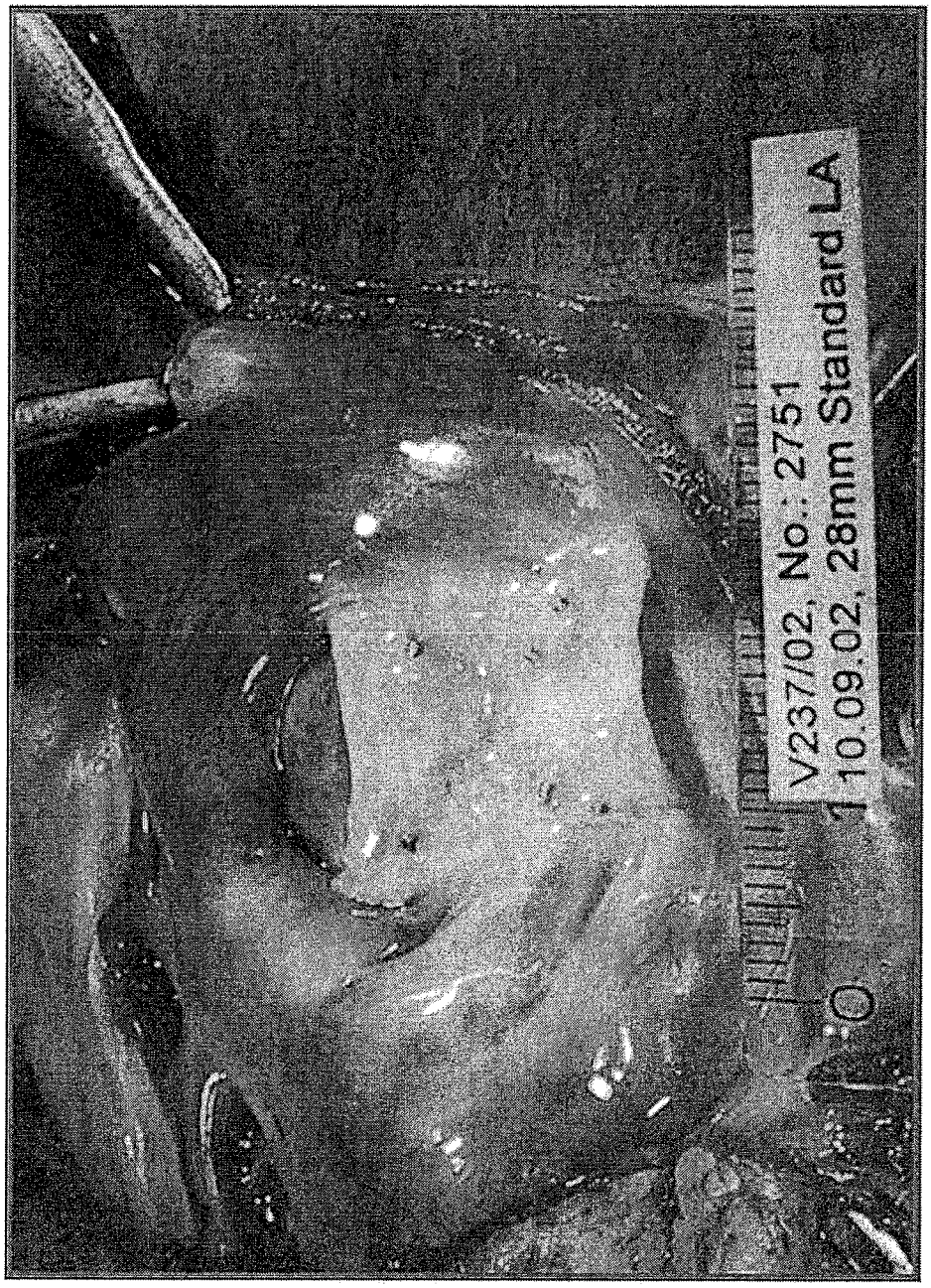

FIG. 7A

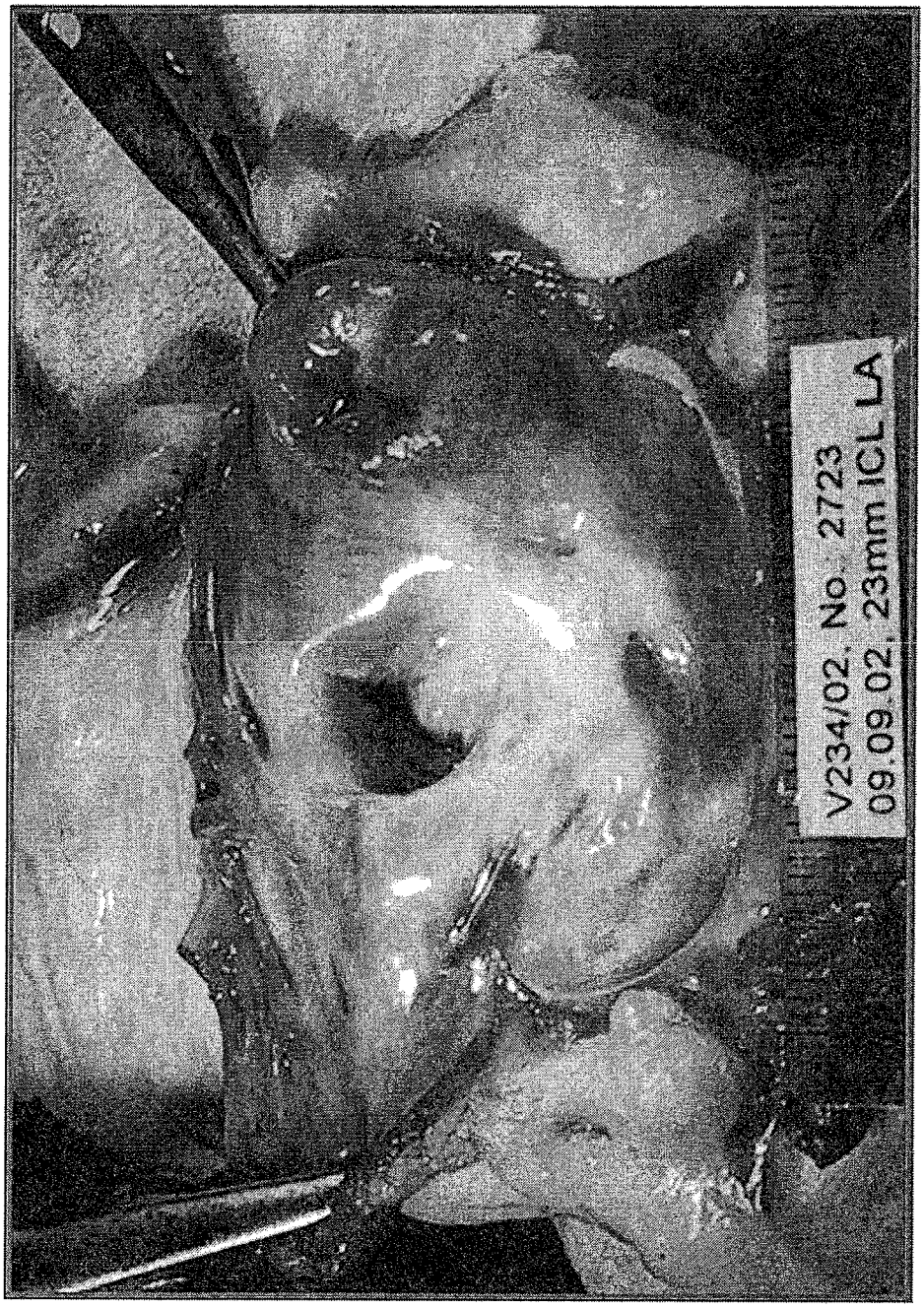

FIG. 7B

DEVICE WITH BIOLOGICAL TISSUE SCAFFOLD FOR PERCUTANEOUS CLOSURE OF AN INTRACARDIAC DEFECT AND METHODS THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a divisional application of U.S. application Ser. No. 11/705,380 filed Feb. 12, 2007, now pending; which is a continuation application of U.S. application Ser. No. 10/453,709 filed Jun. 3, 2003, now abandoned; which claims the benefit under 35 USC §119(e) to U.S. Application Ser. No. 60/385,274 filed Jun. 3, 2002. The disclosure of each of the prior applications is considered part of and is incorporated by reference in the disclosure of this application.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The invention generally relates to devices and related methods for treating intracardiac defects. More particularly, the invention provides an intracardiac occluder with a biological tissue scaffold, and related methods, for the percutaneous closure of intracardiac defects.

2. Background Information

The human heart is divided into four compartments or chambers. The left and right atria are located in the upper portion of the heart and the left and right ventricles are located in the lower portion of the heart. The left and right atria are separated from each other by a muscular wall, the intraatrial septum, while the ventricles are separated by the intraventricular septum.

Either congenitally or by acquisition, abnormal openings, holes, or shunts can occur between the chambers of the heart or the great vessels, causing blood to flow therethrough. Such deformities are usually congenital and originate during fetal life when the heart forms from a folded tube into a four chambered, two unit system. The deformities result from the incomplete formation of the septum, or muscular wall, between the chambers of the heart and can cause significant problems. Ultimately, the deformities add strain on the heart, which may result in heart failure if they are not corrected.

One such deformity or defect, a patent foramen ovale, is a persistent, one-way, usually flap-like opening in the wall between the right atrium and left atrium of the heart. Since left atrial pressure is normally higher than right atrial pressure, the flap typically stays closed. Under certain conditions, however, right atrial pressure exceeds left atrial pressure, creating the possibility for right to left shunting that can allow blood clots to enter the systemic circulation. This is particularly worrisome to patients who are prone to forming venous thrombus, such as those with deep vein thrombosis or clotting abnormalities.

Nonsurgical (i.e., percutaneous) closure of patent foramen ovales, as well as similar intracardiac defects such as atrial septal defects, ventricular septal defects, and left atrial appendages, is possible using a variety of mechanical closure devices. These devices, which allow patients to avoid the potential side effects often associated with standard anticoagulation therapies, typically consist of a metallic structural framework that is combined with a synthetic scaffold material. The synthetic scaffold material encourages ingrowth and encapsulation of the device. Current devices typically utilize a polyester fabric, expanded polytetrafluoroethylene (ePTFE), Ivalon®, or a metal mesh as the synthetic scaffold material. Such devices suffer, however, from several disadvantages, including thrombus formation, chronic inflammation, and residual leaks.

SUMMARY OF THE INVENTION

The present invention provides a device for occluding intracardiac defects. The device includes a biological tissue scaffold, as opposed to a synthetic scaffold (e.g., a polyester fabric, ePTFE, Ivalon®, or a metal mesh) as presently used by devices known in the art. In a preferred embodiment, the biological tissue scaffold is fabricated from collagen. In one embodiment, a specific type of biological tissue, derived from the tunica submucosa layer of the porcine small intestine, forms the tissue scaffold. As a result of this structure, the aforementioned disadvantages associated with the devices known in the art are minimized or eliminated.

In one aspect, the invention provides an intracardiac occluder for percutaneous transluminal treatment of an intracardiac defect. The intracardiac occluder includes a proximal support structure supporting a proximal occlusion shell and a distal support structure supporting a distal occlusion shell. The distal support structure is coupled to the proximal support structure and at least one of the occlusion shells includes a biological tissue scaffold.

Various embodiments of this aspect of the invention include the following features. The biological tissue scaffold may be a purified bioengineered type 1 collagen that may be derived from a tunica submucosa layer of a porcine small intestine. Further, in one embodiment, at least one of the support structures includes a corrosion resistant metal. Alternatively, at least one of the support structures includes a bioresorbable polymer or a biodegradable polymer. In yet another embodiment, the proximal support structure includes a plurality of outwardly extending proximal arms and the distal support structure includes a plurality of outwardly extending distal arms.

In another aspect, the invention provides a method for percutaneous transluminal treatment of an intracardiac defect in a patient. The method includes providing an intracardiac occluder as described above, positioning the intracardiac occluder proximate the intracardiac defect, and engaging the intracardiac defect with the intracardiac occluder to substantially occlude the intracardiac defect.

In one embodiment of this aspect of the invention, the intracardiac defect is engaged by positioning the proximal occlusion shell and the distal occlusion shell on different sides of the intracardiac defect. The intracardiac defect may be, for example, a patent foramen ovale, an atrial septal defect, a ventricular septal defect, or a left atrial appendage.

In yet another aspect, the invention provides a method for making an intracardiac occluder for the percutaneous transluminal treatment of an intracardiac defect. The method includes providing an overall support structure and first and second biological tissue scaffolds. The overall support structure includes a proximal support structure and a distal support structure. The method further includes coupling the first biological tissue scaffold to the proximal support structure and coupling the second biological tissue scaffold to the distal support structure. In various embodiments of this aspect of the invention, the biological tissue scaffolds are sewn, laminated, or glued to the support structures.

The foregoing and other objects, aspects, features, and advantages of the invention will become more apparent from the following description and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, like reference characters generally refer to the same parts throughout the different views. Also, the draw-

ings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the invention.

FIG. **1** is a cutaway view of a heart illustrating an intracardiac defect.

FIG. **2**A is a top plan view of an intracardiac occluder according to an illustrative embodiment of the invention.

FIG. **2**B is a cross-sectional view of the illustrative intracardiac occluder of FIG. **2**A.

FIG. **3**A is a top plan view of an intracardiac occluder according to another illustrative embodiment of the invention.

FIG. **3**B is a side view of the illustrative intracardiac occluder of FIG. **3**A.

FIG. **4** is a perspective view of an intracardiac occluder according to another illustrative embodiment of the invention.

FIGS. **5**A-**5**E illustrate the stages, according to an illustrative embodiment of the invention, for delivering an intracardiac occluder to an anatomical site in the body of a patient.

FIG. **6**A illustrates the results from occluding an intracardiac defect with an intracardiac occcluder known in the art, 30-days after delivery of the intracardiac occluder.

FIG. **6**B illustrates the results from occluding an intracardiac defect with an intracardiac occluder according to the invention, 30-days after delivery of the intracardiac occluder.

FIG. **7**A illustrates the results from occluding an intracardiac defect with an intracardiac occcluder known in the art, 90-days after delivery of the intracardiac occluder.

FIG. **7**B illustrates the results from occluding an intracardiac defect with an intracardiac occcluder according to the invention, 90-days after delivery of the intracardiac occluder.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides an intracardiac occluder for the repair of intracardiac defects, such as, for example, a patent foramen ovale, an atrial septal defect, a ventricular septal defect, and left atrial appendages. The intracardiac occluder includes a structural framework and a biological tissue scaffold adhered thereto.

FIG. **1** depicts a cutaway view of a heart **100**. The heart **100** includes a septum **104** that divides a right atrium **108** from a left atrium **112**. The septum **104** includes a septum primum **116**, a septum secundum **120**, and an exemplary intracardiac defect **124**, which is to be corrected by the intracardiac occluder of the present invention, between the septum primum **116** and the septum secundum **120**. Specifically, a patent foramen ovale **124** is shown as an opening through the septum **104**. The patent foramen ovale **124** provides an undesirable fluid communication between the right atrium **108** and the left atrium **112**. Under certain conditions, a large patent foramen ovale **124** in the septum **104** would allow for the shunting of blood from the right atrium **108** to the left atrium **112**. If the patent foramen ovale **124** is not closed or obstructed in some manner, a patient is placed at high risk for an embolic stroke.

FIG. **2**A depicts an intracardiac occluder **10** according to an illustrative embodiment of the invention. As shown, the intracardiac occluder **10** includes a proximal occlusion shell **18** (i.e., an occlusion shell that is closest to an operator of the intracardiac occluder **10** (e.g., a physician)), an opposite distal occlusion shell **20**, and an overall support structure **16**. The overall support structure **16** includes a proximal support structure **24**, for supporting the proximal occlusion shell **18**, and a distal support structure **34**, for supporting the distal occlusion shell **20**. In one embodiment, both the proximal support structure **24** and the distal support structure **34** include outwardly extending arms to support each of their respective occlusion shells **18**, **20**. As shown in FIG. **2**A, for example, the proximal support structure **24** includes four outwardly extending arms **26** and the distal support structure **34** similarly includes four outwardly extending arms **36**. In one embodiment, each outwardly extending arm is resiliently biased as a result of including three or more resilient coils **43** radially spaced from a center point **45**. Alternatively, other resilient support structures could be used. In one embodiment, the eight arms **26**, **36** are mechanically secured together by wire **52**. Alternatively, other means, such as, for example, laser welding, may be used to secure the eight arms **26**, **36** together. A cross-sectional view of the intracardiac occluder **10** illustrated in FIG. **2**A, showing four arms **26**, **36**, is depicted in FIG. **2**B.

FIGS. **3**A and **3**B depict an intracardiac occluder **10'** according to another illustrative embodiment of the invention. An overall support structure **16'** forms a clip and includes a proximal support structure **24'**, for supporting a proximal occlusion shell **18'**, and a distal support structure **34'**, for supporting a distal occlusion shell **20'**.

An intracardiac occluder **10"** according to yet another illustrative embodiment of the invention is illustrated in FIG. **4**. Again, an overall support structure **16"** forms a clip and includes a proximal support structure **24"**, for supporting a proximal occlusion shell **18"**, and a distal support structure **34"**, for supporting a distal occlusion shell **20"**.

Alternatively, the overall support structure **16** may assume any shape or configuration to form the proximal support structure **24** and the distal support structure **34**.

In one embodiment, the overall support structure **16** is fabricated from a corrosion resistant metal, such as, for example, stainless steel, nitinol, or a nickel-cobalt-chromium-molybdenum alloy (e.g., MP35N). Alternatively, in other embodiments, the overall support structure **16** is fabricated from bioresorbable or biodegradeable polymers.

In accordance with the present invention, the occlusion shells **18**, **20**, which are attached, as described below, to the proximal support structure **24** and the distal support structure **34**, respectively, are made from a biological tissue scaffold. In a preferred embodiment, the tissue scaffold is fabricated from collagen. In one embodiment, a purified (acellular) bioengineered type 1 collagen derived from the tunica submucosa layer of the porcine small intestine forms the tissue scaffold. More specifically, the tunica submucosa layer, referred to hereinafter as the Intestinal Collagen Layer ("ICL"), is separated or delaminated from the other layers of the porcine small intestine (i.e., the tunica muscularis and the tunica mucosa) by any method known in the art. For example, a Bitterling sausage casing machine is used to perform the separation. Once mechanically separated from the other layers, the ICL is, in one embodiment, chemically cleaned to remove debris and other substances, other than collagen. For example, the ICL is soaked in a buffer solution at 4 degrees Celsius without the use of any detergents, or, alternatively, in a second embodiment, it is soaked with NaOH or trypsin. Other cleaning techniques known to those skilled in the art may also be used. After cleaning, the ICL is decontaminated. Any sterilization system for use with collagen, as known in the art, may be used. For example, a dilute peracetic acid solution, gamma sterilization, or electron-beam sterilization is used to decontaminate the ICL.

Alternatively, collagenous tissue from the fascia lata, pericardium, or dura matter of pigs or other mammalian sources, such as, for example, cows or sheep, may form the tissue scaffold. Additionally, in making the occlusion shells **18**, **20**, two or more collagen layers may be bonded together and then

cross-linked to produce a biocompatible material capable of being remodeled by the host cells.

In one embodiment, the biological tissue scaffold is non-porous and prevents the passage of fluids that are intended to be retained by the implantation of the intracardiac occluder **10**. In another embodiment, heparin is ionically or covalently bonded to the biological tissue scaffold to render it non-thrombogenic. In yet other embodiments, proteins or cells are applied to the biological tissue scaffold to render it non-thrombogenic and/or accelerate the healing process. Growth factors may also be applied to the biological tissue scaffold to accelerate the healing process.

Referring again to FIG. **2**A, the occlusion shells **18**, **20** are, in one embodiment, generally square in shape. Alternatively, the occlusion shells **18**, **20** may assume other shapes. The biological tissue scaffold forming the occlusion shells **18**, **20** is strong and flexible. The occlusion shells **18**, **20** therefore easily attach to the overall support structure **16** and, as explained below, withstand sheath delivery to an anatomical site in the body of a patient. In one embodiment, the occlusion shells **18**, **20** are sewn, as at **22**A, **22**B, with any commonly used suture material (e.g., a polyester suture) that threads through the distal ends **54** of the respective arms **26**, **36** of the proximal support structure **24** and the distal support structure **34**. Alternatively, the occlusion shells **18**, **20** are laminated, glued, or attached by, for example, hooks or thermal welding to the proximal support structure **24** and the distal support structure **34**. In yet another embodiment, the occlusion shells **18**, **20** are laminated to the overall support structure **16** and, additionally, to one another, such that the overall support structure **16** is encapsulated entirely within the occlusion shells **18**, **20**.

FIGS. **5**A-**5**E depict the stages for delivering the intracardiac occluder **10**, according to an illustrative embodiment of the invention, percutaneously to an anatomical site in the body of a patient. Referring to FIG. **5**A, a sheath **190** is first inserted into the intracardiac defect **186** as is typically performed by one skilled in the art. The intracardiac occluder **10** is then loaded into the lumen **188** of the sheath **190** and advanced throughout the lumen **188** until positioned at the distal end **192** of the sheath **190**. Referring to FIG. **5**B, the distal occlusion shell **20** of the intracardiac occluder **10** is released into the distal heart chamber **191** through the distal end **192** of the sheath **190**. The distal occlusion shell **20** opens automatically and resiliency. The sheath **190** is then pulled back into the proximal heart chamber **193**, as illustrated in FIG. **5**C, to seat the distal occlusion shell **20** against the distal wall surface **194** of the intracardiac defect **186**. The intracardiac defect **186** is thereby occluded from the distal side. As shown in FIG. **5**D, the sheath **190** is then further withdrawn a sufficient distance to allow the proximal occlusion shell **18** to be released from the distal end **192** of the sheath **190**. The proximal occlusion shell **18** opens automatically and resiliently to lie against the proximal surface **196** of the intracardiac defect **186**, occluding the intracardiac defect **186** from the proximal side. The sheath **190** is then withdrawn from the patient's body, leaving behind the opened intracardiac occluder **10**. As shown in FIG. **5**E, the occlusion shells **18**, **20** are positioned on either side of the intracardiac defect **186** and the intracardiac occluder **10** is permanently implanted within the body of the patient.

FIGS. **6**A-**6**B and **7**A-**7**B depict comparative 30-day and 90-day results, respectively, for the percutaneous closures of interventionally created intracardiac defects in sheep. Specifically, FIGS. **6**A and **7**A depict the 30-day and 90-day results, respectively, when an exemplary intracardiac occluder known in the art, whose occlusion shells were fabricated from a polyester fabric (i.e., a synthetic scaffold material), is used to occlude the intracardiac defect. FIGS. **6**B and **7**B depict the 30-day and 90-day results, respectively, when the intracardiac occluder **10** of the instant invention, whose occlusion shells **18**, **20** were fabricated from ICL, is used to occlude the intracardiac defect.

As shown, the biological tissue scaffold of the intracardiac occluder **10** of the present invention increases the rate of tissue ingrowth and, consequently, decreases the time needed to completely close the intracardiac defect. Specifically, referring now to FIG. **7**B, the intracardiac occluder **10** of the present invention is barely visible after 90-days. The surrounding tissue ingrowth nearly completely envelopes the intracardiac occluder **10**. In comparison, referring now to FIG. **7**A, the exemplary intracardiac occluder known in the art is still clearly visible after the same period of time.

As also shown, the intracardiac occluder **10** of the present invention naturally adheres to, and seals completely along, the edge of the intracardiac defect in a manner that is much improved from the exemplary intracardiac occluder known in the art. Additionally, in one embodiment, the biological tissue scaffold of the intracardiac occluder **10** of the present invention is non-porous. As a result, the intracardiac occluder **10** decreases the likelihood of fluid (e.g., blood) leakage through the opening.

Further advantages to the intracardiac occluder **10** of the present invention, in comparison to known intracardiac occluders, include decreased thrombogenicity, quicker endothelialization, superior biocompatibility, minimal foreign body reaction, decreased inmmunological and inflammatory responses, and no fibrosis.

Variations, modifications, and other implementations of what is described herein will occur to those of ordinary skill in the art without departing from the spirit and the scope of the invention as claimed. Accordingly, the invention is to be defined not by the preceding illustrative description but instead by the spirit and scope of the following claims.

What is claimed is:

1. An intracardiac occluder clip for permanent implantation in the percutaneous transluminal space to treat an intracardiac defect so as to substantially close the intracardiac defect through host tissue endothelialization, said occluder comprising:

a resilient wire forming opposing proximal and distal support structures for occlusion shells, wherein each support structure is formed of two external stems and two internal stems forming a M-shaped arcuate length of the wire, wherein both external stems of each M-shaped support structure are joined to the external stems of the opposing M-shaped support structure;

a proximal occlusion shell providing a scaffold for endothelialization, wherein the shell is formed of a non-porous bioresorbable sheet and is fitted securely between the external and internal stems of the M-shaped proximal support structure; and,

a distal occlusion shell providing a scaffold for endothelialization, wherein the shell is formed of a non-porous bioresorbable sheet and is fitted securely between the external and internal stems of the M-shaped distal support structure.

2. The occluder of claim **1**, wherein the bioresorbable sheet is purified bioengineered type 1 collagen.

3. The occluder of claim **2**, wherein the purified bioengineered type 1 collagen is derived from a tunica submucosa layer of the intestine.

4. The occluder of claim **1**, wherein the wire is fabricated from a corrosion resistant metal.

5. The occluder of claim 1, wherein at the wire is fabricated a bioresorbable polymer.

6. The occluder of claim 1, wherein the wire is fabricated from a biodegradable polymer.

7. The occluder of claim 1, wherein the collagen sheet is treated to be non-thrombogenic.

8. A method for treating a septal defect in a heart, the method comprising:

(a) compressing the occluder of claim 1 into the distal end of a catheter sheath;

(b) introducing the sheath into the heart and through the septal defect to position its distal end on the distal surface of the septal defect;

(c) extending the distal occlusion shell out of the sheath to automatically and resiliently seat the shell against the distal side of the septal defect;

(d) withdrawing the sheath to position its distal end of the sheath at the proximal surface of the septal defect;

(e) extending the proximal occlusion shell out of the sheath to automatically and resiliently seat the shell against the proximal side of the septal defect; and,

(f) releasing the occluder to leave it in the septal defect and withdrawing the sheath from the heart.

9. The method of claim 8, wherein the intracardiac defect is a patent foramen ovale.

10. The method of claim 8, wherein the intracardiac defect is an atrial septal defect.

11. The method of claim 8, wherein the intracardiac defect is a ventricular septal defect.

12. The method of claim 8, wherein the intracardiac defect is a left atrial appendage.

13. The method of claim 8, further comprising step (g), confirming after at least 90 days that endotheliazaiton of the occlusion shells has occurred.

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